

Attorney Docket No. (P3250) 6675.142US1  
Response to Office Action Dated April 11, 2005

Serial No. 09/359,260

### Remarks

#### **I. Introduction**

By the present Amendment, claims 128-130 and 133 have been cancelled, and claims 76, 82-89, 92-95, 131, 132, and 134 amended. Claims 135-138 are newly presented for consideration. Accordingly, claims 76, 82-95, 131, 132, and 134-138 are now pending in the application.

#### **II. Interview Summary**

Applicants and their representatives thank the Examiner for the courtesy and cooperation extended during the interview conducted on June 20, 2005 at the U.S. Patent and Trademark Office. Present at the interview were Examiner Eric S. DeJong, Ph.D., Primary Examiner John S. Brusca, Ph.D., Leonid D. Thenor, and Belinda Lew, Ph.D.

During the interview, Applicants provided a PowerPoint presentation as an overview of the invention and methodology. Claims 76, 82-95, and 128-134 were discussed with respect to all rejections of record. The claims were also discussed with respect to Ostrem et al. Examiner Brusca discussed the manner in which a whole molecule parameter could be interpreted as a sequence-specific parameter if additional amino acids were added or removed from a particular peptide. The term "relationship" was indicated as being broad relative to the disclosure. It was also indicated that the claims did not specify that the second test peptide library could contain members that were not present in the first peptide library. It was indicated that Ostrem identified peptides of different lengths as well as a second library that contained members from the first library. It was also indicated that the specification did not appear to support the term "compound isomer", as recited in claim 129.

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Various possible amendments were discussed that could potentially address issues raised under 35 U.S.C. §112, second paragraph and 35 U.S.C. §102(b). No agreements were reached on claim amendments.

### **III. Summary of Rejections**

In the Office Action of April 11, 2004, the title of the invention was objected to as being non-descriptive of the claimed invention. In response, Applicants have provided a new title which is clearly descriptive of the invention being claimed.

Claims 76, 82-93, and 128-134 were rejected under 35 U.S.C. §112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. Claims 76, 82, 83, 87, 92-95, and 128-134 were rejected under 35 U.S.C. §102(b) as being anticipated by Ostrem et al. The cancellation of claims 128-130 and 133 renders some of these grounds of rejection moot. With respect to the pending claims, these rejections are respectfully traversed.

### **IV. Support for Claim Amendments**

Claims 135-138 have been introduced to more clearly define the invention by addressing, at least in part, some of the issues of new matter raised in the Office Action, and to secure additional coverage for subject matter to which Applicants are entitled protection. Amendments have also been made to reflect proper dependency as a result of cancellation and introduction of claims. Applicants respectfully submit that the new and amended claims are fully supported by the specification. Accordingly, no new matter is added by this Amendment and entry thereof is respectfully requested.

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**V. Rejection under 35 U.S.C. §112, first paragraph**

Claims 76, 82-93, and 128-134 were rejected under 35 U.S.C. §112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. With respect to this rejection, the Office Action indicates, for example, that claim 128 recites the limitation of peptides having a length "no greater than 20 amino acids." The specification is interpreted as providing support for peptides having a "length in a range from about four to about twenty amino acids." The Office Action also indicates that the specification does not provide direct support for combining the steps of claim 129 with those of claim 128.

By the present Amendment, Applicants have canceled claims 128-130, and introduced new claims 135-138. The new claims address all issues raised in the Office Action under §112. For example, claims 135 and 137 recite the range of amino acids identified in the Office Action for the peptide lengths. Claim 136 is newly presented to provide some of the steps of claim 129 in a form that is fully supported by the specification.

Applicants respectfully request withdrawal of this rejection.

During the interview, it was indicated that the term "compound isomer" was not properly supported by the specification. Applicants respectfully disagree, as the specification describes a compound isomer at pages 45 and 46.

**VI. Rejections under 35 U.S.C. §102**

Claims 76, 82, 83, 87, 92-95, and 128-134 were rejected under 35 U.S.C. §102 as anticipated by Ostrem. In support of this rejection, the Office Action provides citation to several

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passages that allegedly disclosed various steps recited in the claims. For example, the Office Action indicates that Ostrem discloses identification of peptides having a length of 8 amino acids, and that such disclosure reads on both the claim limitation of characterizing first test peptides by a first parameter that is sequence-specific, as well as the claim limitation of selecting a plurality of peptides using a space-filling design. The Office Action also indicates that the ability of test combinatorial peptides of 8 amino acids in length to bind with factor Xa reads on the claimed determination of a relationship between the indicia of activity, the first parameter, and the second parameter. Furthermore, the Office Action states identifying a subset of the first test peptide library and, based on their ability to bind factor Xa, using the peptides in a prothrombinase assay reads on the claimed step of identifying a second test peptide library.

While the cancellation of claims 128-130 renders this ground of rejection moot, Applicants respectfully submit that claims 135-138 are patentable over Ostrem. For example, newly presented claim 135 defines a method of identifying a peptide with a desired activity having an indicia that satisfies a test requirement. The method of claim 135 is intended to reduce the actual number of experiments performed when screening peptides for a particular activity, while also maximizing the number of candidate peptides that may potentially have a desired level of the activity. Independent claim 135 recites, in part, the steps of:

- identifying a predetermined set of peptides;
- parameterizing the predetermined set of peptides by:
  - determining a first parameter for each predetermined peptide, wherein the first parameter is a whole molecule parameter, and
  - determining a second parameter for each predetermined peptide, wherein the second parameter is dependent on the specific order of constitutive subunits within each predetermined peptide;
- performing a space-filling design of the parameterized peptides;

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constructing a first test peptide library comprising a plurality of first test peptides identified using the space-filling design, wherein the length of said first test peptides comprises about four amino acids to about twenty amino acids, and wherein said first test peptides are a subset of said predetermined set of peptides;

determining an activity, having an indicia, of said plurality of first test peptides;

measuring the indicia of said activity for said plurality of first test peptides;

deriving a quantitative relationship between said indicia of said activity, said first parameter, and said second parameter;

calculating an estimated indicia for each remaining peptide from said predetermined set of peptides using said quantitative relationship;

setting a test requirement, based on a desired activity, having a test indicia range;

selecting a second test peptide library comprising at least one second test peptide, wherein each second test peptide has an estimated indicia that satisfies said test requirement, and wherein said second test peptides are not in said first test peptide library;

measuring the indicia of each second test peptide; and

identifying at least one second test peptide having a measured indicia that satisfies said test requirement.

According to independent claim 135, a predetermined set of peptides is identified. This would be typically done, for example, by a researcher, scientist, etc. The predetermined peptides are then parameterized through determination of first and second parameters. The first parameter is a whole molecule parameter, while the second parameter depends on the specific order of constitutive subunits within each desired peptide. More particularly, if a peptide contains seven amino acids, then the second parameter would be, for example, a parameter that can take on different values depending on the order of the seven amino acids that make up the peptide. A space-filling design is then performed for the parameterized peptides. A first test peptide library is constructed to include a plurality of first test peptides identified using the space-filling design. The first test peptides are a subset of the predetermined set of peptides and are representative of the parameterized space occupied by the predetermined set of peptides.

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Next, the first test peptides are tested such that an indicia can be measured for a desired activity. The desired activity can correspond, for example, to a particular feature of interest to a user (i.e., scientist, researcher, etc.). This indicia is measured for each first test peptide. A quantitative relationship is then derived based on the measured indicia, the first parameter and the second parameter. Once the quantitative relationship is determined, it is applied to calculate an estimated indicia for each remaining peptide from the predetermined set of peptides. The user then sets a test requirement based on the desired activity. The test requirement is in the form of a range of test indicia values. These values can correspond to a desired range that satisfies a criteria the user considers important. Next, a second test peptide library containing at least one second test peptide is selected. Only second test peptides having an estimated indicia that satisfies the test requirement are selected to be in the second test peptide library. Since the estimated indicia are calculated only for the remaining peptides, none of the second test peptides are present in the first test peptide library. The user then tests the second test peptides in order to measure the actual indicia. Finally, at least one second test peptide that satisfies the test requirement is identified.

The method defined by claim 135 advantageously reduces the amount of experimentation required to identify peptides having a desired indicia as discussed in the "Background" section of the application. This reduction can directly translate to a reduction in time and costs associated with identifying such peptides. Additionally, users are able to generate a substantially large group of candidate peptides that could potentially have an indicia which satisfies the test requirement. The candidate peptides can then be filtered to a smaller number of second test peptides that will actually be tested by properly setting the test requirement. Consequently, the number of actual experiments conducted can be significantly reduced.

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Ostrem, however, does not appear to disclose or suggest, a method of identifying peptides with a desired activity, as set forth in independent claim 135. Ostrem discloses a library for screening of biotinylated factor Xa-SAP mixture added to library beads. Beads that showed a blue color were destained, stripped, and further screened with the factor Xa-SAP-inhibitor mixture. In contrast to the claimed invention, Ostrem does not parameterize the predetermined peptides through determination of first and second parameters. Determining a peptide length of 8 amino acids simply cannot be interpreted as reading on the claimed the step of determining a second parameter which depends on the specific order of constitutive subunits within each desired peptide. Ostrem utilizes a combinatorial library, and does not disclose or suggest any space-filling techniques. Similarly, Ostrem provides no disclosure or suggestion for deriving a quantitative relationship between the measured indicia, the first parameter, and the second parameter. Finally, Ostrem clearly fails to even suggest application of the derived quantitative relationship to calculate an estimated indicia for peptides remaining in the predetermined set of peptides. Rather, the increased potency range of the initial leads identified in the combinatorial library are measured and not calculated from a derived relationship as set forth in the claims.

Applicants therefore respectfully submit that the claims of the present invention are not anticipated by Ostrem, and request withdrawal of the rejection under 35 U.S.C. §102.

Claims 76 and 82-95 depend, either directly or indirectly, from claim 135 and are therefore believed allowable for at least the reasons set forth above with respect to claim 135. In addition, these claims each introduce novel elements that independently render them patentable over the art of record.

Claims 136-138 are newly presented for consideration. These claims also introduce various novel steps that are somewhat similar to the steps recited in independent claim 135.

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These steps are not shown or suggested by the art of record. Accordingly, claims 136-138 are believed allowable over the art of record.

Claims 131, 132, and 134 depend from independent claim 137, and are also believed allowable for at least the reasons set forth above with respect to independent claims 135 and 137.

## **VII. CONCLUSION**

Applicants respectfully submit that, as described above, the cited prior art does not show or suggest the steps recited in the claims. Applicants do not concede that the cited prior art shows any of the steps recited in the claims. However, Applicants have provided specific examples of steps in the claims that are clearly not present in the cited prior art.

For all the reasons advanced above, Applicants respectfully submit that the rejections have been overcome and should be withdrawn.

For all the foregoing reasons, Applicants respectfully submit that all of the pending claims are now in condition for allowance, and a Notice of Allowance is courteously solicited.

The Examiner is respectfully requested to contact the undersigned, to schedule an interview if it is believed that such contact would further the examination of the present application.



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**AUTHORIZATION**

The Commissioner is hereby authorized to charge any additional fees which may be required for this Amendment, or credit any overpayment to deposit account no. 08-0219.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to deposit account no. 08-0219.

Respectfully Submitted,

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